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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/518,751	06/19/2006	Brad St Croix	001107.00526	8976

22907 7590 06/20/2008

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EXAMINER	
BLANCHARD, DAVID J	

ART UNIT	PAPER NUMBER
1643	

MAIL DATE	DELIVERY MODE
06/20/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/518,751	ST CROIX ET AL.	
	Examiner	Art Unit	
	David J. Blanchard	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *1* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 October 2007*.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *55-108* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *55-108* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. In a telephonic conversation on 18 June 2008, Applicant pointed out that the restriction requirement mailed 11 June 2008 did not properly set forth Groups of inventions pertaining to pending claims 55-108 and requested clarification. The Examiner notes that the restriction mailed 11 June 2008 was sent in error and is hereby VACATED in favor of the instant restriction requirement, which corrects the inconsistencies of the restriction requirement mailed 11 June 2008. The period for reply begins on the mail date of the instant Office Action.

2. Applicant is advised that multiple elections are required as set forth below. Applicant is required to elect one of the categories of Inventions I-XXVI and one recited TEM protein (see item no. 4 below).

Election/Restrictions

3. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions, which are not so linked as to form a single general inventive concept under PCT Rule 13.1. To have a general inventive concept under PCT rule 13.1, the inventions need to be linked by a special technical feature. The special technical feature recited in claim 1 is an isolated molecule comprising an antibody variable regions which specifically binds to an extracellular domain of a TEM protein recited in claim1. In view of this Yauch R. L. et al. (The Journal of Biological Chemistry, 275(13):9230-9238, March 13, 2000, cited on PTO-892 mailed 6/11/08) reads on the claim. Yauch et al teaches a monoclonal antibody that binds to the extracellular domain of the TEM protein CD151. Therefore the technical feature recited in claim 1 is not special. Accordingly the groups are not so linked as to form a single general concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in response to this action, to elect a single invention to which the claims must be restricted.

Group I, claims 55-63, drawn to an antibody that binds the extracellular domain of a transmembrane (TEM) protein.

Group II, claims 64-65 and 70, drawn to a method of inhibiting neoangiogenesis in subject having cancer comprising administering an antibody that binds the extracellular domain of a TEM protein.

Group III, claims 64 and 66, drawn to a method of inhibiting neoangiogenesis in subject having polycystic kidney disease comprising administering an antibody that binds the extracellular domain of a TEM protein.

Group IV, claims 64 and 67, drawn to a method of inhibiting neoangiogenesis in subject having diabetic retinopathy comprising administering an antibody that binds the extracellular domain of a TEM protein.

Group V, claims 64 and 68, drawn to a method of inhibiting neoangiogenesis in subject rheumatoid arthritis comprising administering an antibody that binds the extracellular domain of a TEM protein.

Group VI, claims 64 and 69, drawn to a method of inhibiting neoangiogenesis in subject having psoriasis comprising administering an antibody that binds the extracellular domain of a TEM protein.

Group VII, claims 71-78, drawn to a method of identifying a ligand involved in endothelial cell regulation comprising contacting a TEM protein with a test compound and an antibody that binds the extracellular domain of said TEM, whereby a test compound which diminishes antibody binding to the TEM is identified as a ligand in endothelial cell regulation.

Group VIII, claims 79-81, drawn to a method of identifying a ligand involved in endothelial cell regulation comprising contacting a test compound with a TEM protein, determining binding of the test compound and the test compound which binds to the protein as a ligand involved in endothelial cell regulation.

Group IX, claims 82-83, drawn to a soluble form of a TEM protein, lacking the transmembrane domain

Group X, claims 84-85, drawn to a method of inhibiting neoangiogenesis in subject having cancer comprising administering a soluble form of a TEM protein, lacking the transmembrane domain.

Group XI, claims 84 and 86, drawn to a method of inhibiting neoangiogenesis in subject having polycystic kidney disease comprising administering a soluble form of a TEM protein, lacking the transmembrane domain.

Group XII, claims 84 and 87, drawn to a method of inhibiting neoangiogenesis in subject having diabetic retinopathy comprising administering a soluble form of a TEM protein, lacking the transmembrane domain.

Group XIII, claims 84 and 88, drawn to a method of inhibiting neoangiogenesis in subject rheumatoid arthritis comprising administering a soluble form of a TEM protein, lacking the transmembrane domain.

Group XIV, claims 84 and 89, drawn to a method of inhibiting neoangiogenesis in subject having psoriasis comprising administering a soluble form of a TEM protein, lacking the transmembrane domain.

Group XV, claim 90, drawn to a method of identifying regions of neoangiogenesis in patient comprising administering a detectably labeled antibody that binds the

extracellular domain of a TEM protein, detecting the bound antibody in the patient, thereby identifying regions of neoangiogenesis in the patient.

Group XVI, claim 91, drawn to a method of screening for neoangiogenesis in patient comprising contacting body fluid collected form the patient with an antibody that binds the extracellular domain of a TEM protein, detecting material in the body fluid, wherein detection of material indicates neoangiogenesis.

Group XVII, claims 92-94, drawn to a method to identify candidate drugs for treating tumors or wounds comprising contacting a test compound with cells expressing one or more TEM genes, determining the amount of expression of said one or more TEM genes by hybridization of mRNA of said cancer cells or cDNA or cRNA copied from said mRNA to a nucleic acid probe complementary to an mRNA of said one or more TEM genes, identifying a test compound as a candidate drug for treating tumors or wounds if it decreases expression of said one or more TEM genes.

Group XVIII, claims 95-97, drawn to a method to identify candidate drugs for treating tumors or wounds comprising contacting a test compound with cells expressing one or more TEM proteins, determining the amount of said one or more TEM proteins, identifying a test compound as a candidate drug for treating tumors or wounds if it decreases the amount of said one or more TEM proteins.

Group XIX, claims 98-100, drawn to a method to identify candidate drugs for treating tumors or wounds comprising contacting a test compound with cells expressing one or more TEM proteins, determining the activity of said one or more TEM proteins, identifying a test compound as a candidate drug for treating tumors or wounds if it decreases the activity of said one or more TEM proteins.

Group XX, claim 101, drawn to a method to identify candidate drugs for treating tumors or wounds comprising contacting a test compound with recombinant host cells which

are transfected with an expression vector which encodes one or more TEM proteins, determining the amount of proliferation of said cells, identifying a test compound as a candidate drug for treating tumors if it inhibits proliferation of said cells or identifying a test compound which stimulates proliferation of said cells as a candidate drug for promoting would healing.

Group XXI, claims 102-104, drawn to a method of identifying endothelial cells comprising contacting a population of cells with one or more antibodies that binds a TEM protein, detecting cells in the population which have bound to said molecules, identifying cells which are bound to said one or more antibodies as endothelial cells.

Group XXII, claim 105, drawn to a method of identifying endothelial cells comprising contacting cDNA or mRNA of a population of cells with one or more nucleic acid hybridization probes which are complementary to a cDNA or mRNA for a TEM gene, detecting cDNA or mRNA which have hybridized to dais nucleic acid hybridization probes, identifying cells whose nucleic acids have hybridized to said nucleic acid probes as endothelial cells

Group XXIII, claim 106 in part and claim 107, drawn to a method for inducing an immune response to a TEM protein in a mammal comprising administering to a subject at risk of developing a tumor a TEM protein, whereby a cellular or humoral immune response to the TEM protein is raised in the subject.

Group XXIV, claim 106 in part and claim 107, drawn to a method for inducing an immune response to a TEM protein in a mammal comprising administering to a subject at risk of developing a tumor a nucleic acid encoding a TEM protein, whereby a cellular or humoral immune response to the TEM protein is raised in the subject.

Group XXV, claim 108 in part, drawn to a method of stimulating vascular proliferation comprising administering to a subject with a wound a TEM protein, whereby wound healing is promoted.

Group XXVI, claim 108 in part, drawn to a method of stimulating vascular proliferation comprising administering to a subject with a wound a nucleic acid encoding a TEM protein, whereby wound healing is promoted.

4. Each of the invention categories set forth above (i.e., Groups I-XXVI above) are drawn to numerous patentably distinct TEM proteins (e.g., see claim 55). Therefore, restriction to one (1) of the recited TEM proteins (e.g., see claim 55) is also required under 35 U.S.C. 121. Therefore, Applicant is required to elect one of the recited TEM proteins for each of the invention categories I-XXVI above. Applicants' response to the instant election/restriction requirements should clearly identify one of inventions I-XXVI and one of the recited TEM proteins.

Inventions I-XXVI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP 806.04, MPEP 808.01). In the instant case the different inventions represent structurally different TEM proteins, that have different modes of operation, different functions and different effects. For example, within invention category I, an antibody to a potassium inwardly-rectifying channel would not necessarily bind the CD164 antigen, for example.

5. The inventions listed as Groups I-XXVI do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: As set forth above, in view of the teaching of Yauch et al the groups are not so linked as to form a single general concept under PCT Rule 13.1 because the technical feature of claim 1 is not special.

Inventions of Groups I and IX represent separate and distinct products which are made by materially different methods, and are used in materially different methods which have different modes of operation, different functions and different effects. The antibodies of Group I and the soluble TEM proteins of Group II are all structurally and chemically different from each other. The antibodies are raised by immunization and the TEM proteins are synthesized from mRNA. Furthermore, the antibody can be used to immunopurify the antigen and the soluble TEM proteins can be used to raise antibodies, for example. The examination of all Groups would require different searches in the U.S. Patent shoes and the scientific literature and would require the consideration of different patentability issues. Thus the inventions I and IX are patentably distinct.

The methods of Inventions II-VIII and X-XXVI differ in the method objectives, method steps and parameters and in the reagents used. Inventions II-VI recite to methods of inhibiting neoangiogenesis in subject having cancer, polycystic kidney disease, diabetic retinopathy, rheumatoid arthritis, or psoriasis, respectively, comprising administering an antibody that binds the extracellular domain of a TEM protein; Invention VII recites a method of identifying a ligand involved in endothelial cell regulation comprising contacting a TEM protein with a test compound and an antibody that binds the extracellular domain of said TEM, whereby a test compound which diminishes antibody binding to the TEM is identified as a ligand in endothelial cell regulation; Invention VIII recites a method of identifying a ligand involved in endothelial cell regulation comprising contacting a test compound with a TEM protein, determining binding of the test compound and the test compound which binds to the protein as a ligand involved in endothelial cell regulation; Inventions X-XIV recite methods of inhibiting neoangiogenesis in subject having cancer, polycystic kidney disease, diabetic retinopathy, rheumatoid arthritis, or psoriasis, respectively, comprising administering a soluble form of a TEM protein, lacking the transmembrane domain; Invention XV recites a method of identifying regions of neoangiogenesis in patient comprising administering a detectably labeled antibody that binds the extracellular domain of a TEM protein, detecting the bound antibody in the patient, thereby identifying regions of

neoangiogenesis in the patient; Invention XVI recites a method of screening for neoangiogenesis in patient comprising contacting body fluid collected form the patient with an antibody that binds the extracellular domain of a TEM protein, detecting material in the body fluid, wherein detection of material indicates neoangiogenesis; Invention XVII recites a method to identify candidate drugs for treating tumors or wounds comprising contacting a test compound with cells expressing one or more TEM genes, determining the amount of expression of said one or more TEM genes by hybridization of mRNA of said cancer cells or cDNA or cRNA copied from said mRNA to a nucleic acid probe complementary to an mRNA of said one or more TEM genes, identifying a test compound as a candidate drug for treating tumors or wounds if it decreases expression of said one or more TEM genes; Invention XVIII recites a method to identify candidate drugs for treating tumors or wounds comprising contacting a test compound with cells expressing one or more TEM proteins, determining the amount of said one or more TEM proteins, identifying a test compound as a candidate drug for treating tumors or wounds if it decreases the amount of said one or more TEM proteins; Invention XIX recites a method to identify candidate drugs for treating tumors or wounds comprising contacting a test compound with cells expressing one or more TEM proteins, determining the activity of said one or more TEM proteins, identifying a test compound as a candidate drug for treating tumors or wounds if it decreases the activity of said one or more TEM proteins; Invention XX recites a method to identify candidate drugs for treating tumors or wounds comprising contacting a test compound with recombinant host cells which are transfected with an expression vector which encodes one or more TEM proteins, determining the amount of proliferation of said cells, identifying a test compound as a candidate drug for treating tumors if it inhibits proliferation of said cells or identifying a test compound which stimulates proliferation of said cells as a candidate drug for promoting would healing; Invention XXI recites a method of identifying endothelial cells comprising contacting a population of cells with one or more antibodies that binds a TEM protein, detecting cells in the population which have bound to said molecules, identifying cells which are bound to said one or more antibodies as endothelial cells; Invention XXII recites a method of identifying endothelial cells

comprising contacting cDNA or mRNA of a population of cells with one or more nucleic acid hybridization probes which are complementary to a cDNA or mRNA for a TEM gene, detecting cDNA or mRNA which have hybridized to dais nucleic acid hybridization probes, identifying cells whose nucleic acids have hybridized to said nucleic acid probes as endothelial cells; Inventions XXIII and XXIV recite methods for inducing an immune response to a TEM protein in a mammal comprising administering to a subject at risk of developing a tumor a TEM protein, or a nucleic acid encoding a TEM protein, respectively, whereby a cellular or humoral immune response to the TEM protein is raised in the subject; Inventions XXV and XXVI recite methods of stimulating vascular proliferation comprising administering to a subject with a wound a TEM protein, or a nucleic acid encoding a TEM protein, respectively, whereby wound healing is promoted.

The inventions of Groups II-VIII and X-XXVI are directed to methods that recite structurally and functionally distinct elements and are not required one for the other. The inventions of Groups II-VII, XV-XVI and XXI require an antibody that binds a TEM protein, which is not required by any of the other groups. The inventions of Groups VIII, X-XIV, XXIII and XXV require a TEM protein, which is not required by any of the other groups. The inventions of Groups XXIV and XXVI require a nucleic acid encoding a TEM protein, which is not required by any of the other groups. The examination of all groups would require different searches in the U.S. Patent shoes and the scientific literature and would require the consideration of different patentability issues. Thus Inventions II-VIII and X-XXVI are separate and distinct in having different method objectives, method steps, parameters and reagents used and different endpoints and are patentably distinct.

Inventions I and II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the antibody of Group I can be used in a materially different method such as to purify the antigen in addition to the

materially different therapeutic and diagnostic methods of Groups II-VII, VX-XVI and XXI.

Inventions IX and X are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the soluble TEM protein of Group IX can be used in a materially different method such as to produce antibodies in addition to the materially different therapeutic and diagnostic methods of Groups VIII, X-XIV, XXIII and XXV.

6. Restriction for examination purposes as indicated is proper because all these inventions listed in this action are independent or distinct for the reasons given above and there would be a serious search and examination burden if restriction were not required because one or more of the following reasons apply:

(a) the inventions have acquired a separate status in the art in view of their different classification;
(b) the inventions have acquired a separate status in the art due to their recognized divergent subject matter;
(c) the inventions require a different field of search (for example, searching different classes/subclasses or electronic resources, or employing different search queries);
(d) the prior art applicable to one invention would not likely be applicable to another invention;
(e) the inventions are likely to raise different non-prior art issues under 35 U.S.C. 101 and/or 35 U.S.C. 112, first paragraph.

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a invention to be examined even though the requirement may be traversed (37 CFR 1.143) **and (ii) identification of the claims encompassing the elected invention.**

The election of an invention may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election

shall be treated as an election without traverse. Traversal must be presented at the time of election in order to be considered timely. Failure to timely traverse the requirement will result in the loss of right to petition under 37 CFR 1.144. If claims are added after the election, applicant must indicate which of these claims are readable on the elected invention.

If claims are added after the election, applicant must indicate which of these claims are readable upon the elected invention.

Should applicant traverse on the ground that the inventions are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

7. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. *Process claims that depend from or otherwise include all the limitations of the patentable product* will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims

and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. Failure to do so may result in a loss of the right to rejoinder.

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The examiner can normally be reached at Monday through Friday from 8:00 AM to 6:00 PM, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached at (571) 272-0832.

The official fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/David J. Blanchard/
Primary Examiner, A.U. 1643